(1953), Braude *et al.* (1953), McEntegart (1956), and others after the transfusion of contaminated blood. The blood in those cases was contaminated by cold-growing micro-organisms, most of them Gram-negative. The effects of endotoxins of Gram-negative bacteria have been extensively studied in animals. The main manifestations were fever, diarrhoea and vomiting, hypoglycaemia, changes in leucocyte distribution, and shock, resulting in death. Ebert *et al.* (1955) injected meningococcus toxins intravenously into dogs, producing a precipitous fall in blood pressure. They concluded that this was due to venous pooling of the blood in the viscera. The shock was treated successfully with noradrenaline. Augmentation of the blood volume was less effective, and cortisone was of no help. Weil *et al.* (1956) produced shock in dogs with coli endotoxin. They also explained this phenomenon by venous pooling and were able to correct it by metaraminol.

The role of adrenal damage or insufficiency in the production of shock in those cases of acute septicaemia seems to be of less importance than previously thought. Of the various necropsy reports of fatal contaminated transfusion reactions only one case showed unilateral adrenal damage (McEntegart, 1956). None of the dogs in the experiments of Ebert *et al.* (1955) showed gross adrenal lesions. Although no extensive studies in this direction were done in our patients, results of serum sodium and potassium estimations did not point to adrenal insufficiency.

The severity of the shock seems to be in direct proportion to the quantity of endotoxins introduced into the blood stream. The effect is the same whether the bacteria are dead or alive. The endotoxins of most of the Gram-negative bacilli have the same action—for example, the meningococcus and *E. coli*.

The fatality rate in reported transfusion accidents due to contaminated blood is quite high, especially when Gram-negative bacilli are concerned. Stevens *et al.* (1953) report 32 cases assembled from the literature, including their own, of which 65% ended fatally. Two fatal cases are described by McEntegart (1956).

All our patients recovered. As the reactions began in the early hours of the afternoon, at a time when all the doctors were in the ward, and occurred almost simultaneously, immediate attention was directed to them and treatment was started early. Within 30 to 45 minutes of the beginning of the reaction all the patients in shock were being given noradrenaline drips.

In our opinion this early treatment is one of the main factors that contributed to the recovery, the importance of the time factor in shock being well known. Another factor, not given to comparison or measurement, is the quantity of endotoxins introduced.

The amount of noradrenaline given was not great, an average of 20 mg. per 24 hours being sufficient. Cortisone was found to be of definite value, probably owing to its potentiating effect on noradrenaline, as experimentally demonstrated by Kurland and Freedberg (1951), although, as mentioned above, it has no direct effect on the shock.

Antibiotics were started only the day after the beginning of the reaction and did not seem to play an important part in the treatment.

Because of the severity and potential dangers of this condition no effort should be spared in its prevention. Since no macroscopic abnormalities can be seen in the contaminated solutions, the strictest control of sterilization procedures is essential, with sterility checks of every batch of fluids before distribution.

Summary

Five cases of mild to severe shock due to the intravenous infusion of Darrow's solution contaminated with coliform bacteria are reported. Attention is called to the rapid though masked onset of circulatory collapse, and its mechanism discussed. All patients were successfully

treated with noradrenaline and cortisone. The importance of early recognition and treatment of the shock is emphasized.

We thank Dr. Ch. Sheba, director of Tel Hashomer Hospital and head of the Department of Internal Medicine "C," for helpful advice and encouragement, and Mrs. H. Becker, from the Department of Bacteriology, for technical assistance.

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Medical Memorandum

Incontinentia Pigmenti (Bloch-Sulzberger)

Incontinentia pigmenti is a rare developmental anomaly involving the skin and other ectodermal tissues. The first case under this name was described by Bloch (1926) and again by Sulzberger (1928), though in 1925 Bardach had reported two cases of an identical condition under the diagnosis of systematized naevus formation. In view of the apparent rarity of the condition the following three cases are described.

CASE 1

A female infant, the fifth child of healthy parents, was born after a short labour. During pregnancy the mother had suffered from hyperemesis and mild toxæmia. The birth weight was 7½ lb. (3.4 kg.). Soon after birth a slight discharge was noticed from both eyes; otherwise the child appeared normal. On the second day she developed a generalized rash, and the following day there was twitching of the right arm and right side of the face; as a result of this she was admitted to hospital.

On examination a rash was seen over her trunk and limbs: this consisted of raised erythematous areas, some surmounted with papules and some with pustules. Certain of these erythematous areas showed desquamation and yellow-brown pigmentation (Fig. 1). In addition there was twitch-

FIG. 1.—Case 1, showing the appearance of the skin lesions.

ing of the right arm and right side of the face; the cry was cerebral in type. No other abnormality was found.

A diagnosis was made of cerebral birth trauma with an associated infective erythema, and treatment was begun with phenobarbitone and chlortetracycline. The twitching soon ceased but the rash persisted. Because of this failure

to respond to treatment and the rather unusual appearance of the lesions the baby was seen by the dermatologist, and incontinentia pigmenti was diagnosed.

When she was seen in the out-patient department at the age of 2 months the erythematous areas had almost disappeared, but linear verrucous growth had developed on the legs and feet: there was no evidence of pigmentation. Attempts to persuade the mother to bring the baby back for further examination have not been successful, but she has reported that the child is well and that the skin is clear.

CASES 2 AND 3

These patients were female twins born four years ago; their birth weights were 5 lb. 12½ oz. and 5 lb. 3½ oz. (2.62 and 2.37 kg.) respectively. The delivery was uneventful and no abnormalities were noticed at birth in either infant. At the age of 1 month they both developed sore buttocks, and two weeks later blisters of various sizes appeared on their legs, most of which subsequently burst.

On admission they had an identical skin condition consisting of pemphigus-like blisters; many of these had broken and the raw areas were covered by a dry slough. These lesions occurred over most of the body from the waist downwards. The areas of the skin not affected were erythematous and thickened, and warty growths were found adjacent to the anus. No other abnormality was found in either baby. The appearance of the rash suggested the possibility of syphilis, but the Wassermann tests of the mother and twins were all negative, and no spirochaetes were seen in swabs taken from the lesions. A diagnosis of incontinentia pigmenti was suggested, and a skin biopsy from the left leg of Case 2 was reported on as follows: "There is a flattening of the dermo-epidermal border, and only in a few places short epidermal pegs are seen. There are no pigment granules in the basal layers of the epidermis. In the cutis vera there are numerous fusiform and spider-shaped cells with finely granular acidophil cytoplasm. Only exceptionally brown pigment granules are seen in such cells. A silver impregnation showed somewhat more argentophil granules in these cells. The findings are compatible with the diagnosis of incontinentia pigmenti" (Fig. 2).

Fig. 2.—Case 2. Photomicrograph of skin showing the melanin-containing chromatophores in the corium.

After discharge from hospital the skin condition recurred several times during the first year, but both babies have been completely clear for the past two years. At their last examination neither child had any residual rash or pigmentation, or any evidence of alopecia or dental hypoplasia.

DISCUSSION

The first case of incontinentia pigmenti in this country was described by Haber (1948, 1949). Carney (1951) was able to find 32 cases in the literature; to these he added a further five. Franklin (1952) also reviewed the literature

and added a case of his own, and Kitamura *et al.* (1954) described 21 hitherto unreported cases from Japan. Other papers on the subject are those of Loveman *et al.* (1952), Epstein *et al.* (1952), and Bambridge (1953).

Incontinentia pigmenti occurs predominantly in female infants. All the 21 cases of Kitamura *et al.* (1954) were females, as were 33 of the 37 cases reviewed by Carney (1951).

The condition is often present at birth, but may appear at any time during the first two years. The initial lesion is usually an erythematous rash with superimposed bullae and papules, tending to develop in lines and patches, and may be mistaken for a septic skin condition. This stage tends to persist for weeks or months, with periodic improvement and relapse. Finally, areas of pigmentation appear, either direct from the initial bullous lesions or through an intermediate stage in which linear warty growths develop.

The fully developed condition consists of irregularly scattered areas of slaty-grey or chocolate-brown pigmentation arranged in a series of lines, whorls, and spider formations. These lines do not correspond to nerves or blood vessels, and may cross the midline. In a few cases this is present at birth. The pigmentation tends to fade gradually, but the length of time varies. The course of Cases 2 and 3 would suggest that in some instances definite skin pigmentation does not always appear. In Case 1 it is presumed that this may develop later, as the child is still only 5 months old.

Other ectodermal and mesodermal developmental abnormalities may be associated with the skin pigmentation: alopecia, mental retardation, congenital heart disease, various paralyses, and frequently deficient dentition have all been reported. Occasionally there is a familial history, the disease having been recorded in twins and also in a father and his two daughters (Naegeli, 1927).

The aetiology remains obscure. Bloch (1926) considered that incontinence of the basal cells of the epidermis allowed the melanin to diffuse into the corium, where it was gathered up by the chromatophores. Haber (1952) suggested the possibility that the condition was due to a viral infection of the mother during pregnancy.

The histology of the three stages has been adequately described by Carney (1951). In the early erythematous stage microscopy shows a non-specific acute inflammatory reaction with vesiculation. The epidermal vesicles are often filled with polymorphonuclear eosinophils. The basal-cell layer contains only small amounts of melanin. Examination of one of the verrucous lesions shows hyperkeratosis and acanthosis typically.

The histology of the final pigmented stage shows a diminution or absence of pigment in the basal layers of the epidermis but a relatively large amount of melanin in the chromatophores of the corium. Usually there is associated thinning of the overlying epidermis.

Incontinentia pigmenti is a benign condition and treatment is not required. Findlay (1952) reported the disappearance of the skin lesions with cortisone, although they had returned within three months of stopping treatment.

I thank Dr. Frances Braid and Professor J. M. Smellie for permission to publish these cases; Dr. B. C. Tate for his help and advice in the preparation of this paper; Dr. H. S. Baar for the histological report; and Mr. J. G. Williamson for the photographs.

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